IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Michael D. Culler et al. Art Unit :
Serial No. : Examiner :
Filed : Herewith
Title : METHODS OF INHIBITING FIBROSIS WITH A SOMATOSTIN AGONIST

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the Specification:

On page 1, after the title, insert the following paragraph:

-- Cross Reference to Related Applications

This application is a divisional of application serial number 09/254,097, filed May 10, 1999, now allowed.--

In the Claims:

Cancel claims 144-172 without prejudice.

REMARKS

The present application is a divisional of, and claims priority from, U.S. Patent Application 09/254,097, now allowed. Claims 142 and 143 are now pending.

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Samantha Bell
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Prompt examination of this application, as amended, is respectfully requested.

Please apply any other charges to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 1-16-01

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Michael D. Culler et al. Art Unit:
Serial No.: Examiner:
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Title : METHOD OF INHIBITING FIBROSIS WITH A SOMATOSTATIN AGONIST

Box PCT

Assistant Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the Claims:

Delete claims 1 through 141 and insert new claims 142 through 172.

-- 142. A method of inhibiting fibrosis in a patient said method comprising administering a therapeutically effective amount of somatostatin or a somatostatin agonist to said patient.

143. A method of claim 142, wherein said method comprises administering a therapeutically effective amount of a somatostatin agonist to said patient.

144. A method of claim 143, wherein said fibrosis is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ and or in the gastro-intestinal system.

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Jason Kurian

Jason Kurian

145. A method of claim 143, wherein said fibrosis is induced by chemotherapy, induced by radiation, induced by a drug or a combination of drugs, induced by a disease state, induced by an environmental or an industrial factor, induced by an immune reaction, or induced by a wound.

146. A method of claim 143, wherein said somatostatin agonist is administered parenterally.

147. A method of claim 146, wherein said somatostatin agonist is administered in a sustained release formulation.

148. A method of claim 144, wherein said somatostatin agonist is administered parenterally.

149. A method of claim 148, wherein said somatostatin agonist is administered in a sustained release formulation.

150. A method of claim 143, wherein said somatostatin agonist is administered topically or orally.

151. A method according to claim 144 wherein the fibrotic disorder in the kidney is glomerulonephritis, diabetic nephropathy, allograft rejection or HIV nephropathy; the fibrotic disorder in the lung is idiopathic fibrosis or autoimmune fibrosis; the fibrotic disorder in the liver is cirrhosis or veno-occlusive disease; the fibrotic disorder in the skin is systemic sclerosis, keloids, burn scars or eosinophilia-myalgia syndrome and the fibrotic disorder in the central nervous system is intraocular fibrosis.

152. A method according to claim 145 wherein the fibrosis induced by chemotherapy is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone

or bone marrow, in the cardiovascular system, in an endocrine organ or in the gastro-intestinal system.

153. A method according to claim 145 wherein the fibrosis induced by radiation is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ or in the gastro-intestinal system.

154. A method of inhibiting over-expression of TGF-J which comprises administering to a subject an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

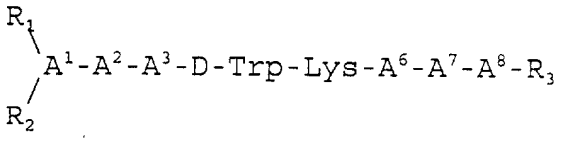
155. A method according to claim 154 wherein a somatostatin agonist or a pharmaceutically acceptable salt thereof is administered.

156. A method according to claim 155 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1, has a higher binding affinity for human somatostatin sub-type receptor 2, has a higher binding affinity for human somatostatin sub-type receptor 3, has a higher binding affinity for human somatostatin sub-type receptor 4, or has a higher binding affinity for human somatostatin sub-type receptor 5.

157. A method according to claim 155 wherein the somatostatin agonist has a higher binding affinity for two or more of human somatostatin sub-type receptor 1, human somatostatin sub-type receptor 2, human somatostatin sub-type receptor 3, human

somatostatin sub-type receptor 4 or human somatostatin sub-type receptor 5.

158. A method according to claim 155 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof, wherein

A^1 is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, J-Nal, J-Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^2 is Ala, Leu, Ile, Val, Nle, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^3 is pyridyl-Ala, Trp, Phe, J-Nal, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^6 is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A^7 is Ala, Leu, Ile, Val, Nle, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^8 is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

each R_1 and R_2, independently, is H, lower acyl or lower alkyl; and R_3 is OH or NH_2; provided that at least one of A^1 and A^8 and one of A^2 and A^7 must be an aromatic amino acid; and further provided that A^1, A^2, A^7 and A^8 cannot all be aromatic amino acids.

159. A method according to claim 155 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH_2;

H-D-Phe-p-NO_2-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-J-D-Nal-NH_2;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-b-Nal-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys-b-Nal-NH_2;

D-b-Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH_2;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Ac-D-Phe-Lys*-Tyr-D-Trp-Lys-Val-Asp-Thr-NH_2, wherein an amide bridge is between Lys* and Asp;

Ac-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-L-hArg(Et)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

Ac-L-hArg(CH_2-CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHEt;

Ac-hArg(CH_3, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-hArg(hexyl$_2$)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Propionyl-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys(iPr)-Thr-Cys-Thr-NH_2;

Ac-D-J-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg(Et)$_2$-NH_2;

Ac-D-Lys(iPr)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Ac-D-hArg(Et)$_2$-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-b-Nal-NH_2;

H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Ac-D-b-Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-Phe-Cys-b-Nal-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH_2;

cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe);

cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe);

cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe);

cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe);
cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Ser-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe);
cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr);
cyclo (Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Pro-Phe-D-Trp-4-Amphe-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba);
cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH$(CH_2)_4$CO);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-b-Ala);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp(NO_2)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba);
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);

cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba);

cyclo (Phe-Phe-D-Trp(5F)-Lys-Thr-Phe-Phe-Gaba);

cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-$(CH_2)_3$-CO);

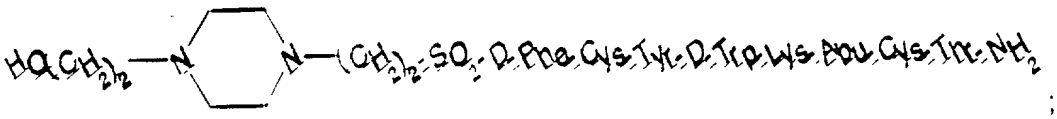
cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);

cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);

cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);

D-b-Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH_2;



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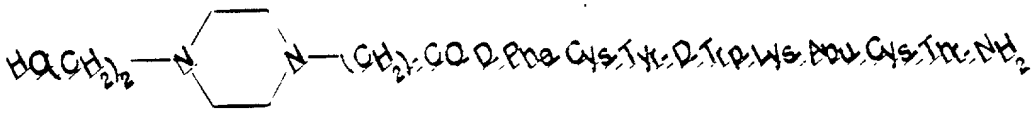


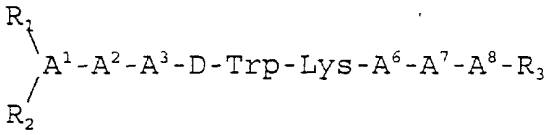
;

or D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys)-Thr-ol; or a pharmaceutically acceptable salt thereof.

160. A method according to claim 143 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1, has a higher binding affinity for human somatostatin sub-type receptor 2, has a higher binding affinity for human somatostatin sub-type receptor 3, has a higher binding affinity for human somatostatin sub-type receptor 4, or has a higher binding affinity for human somatostatin sub-type receptor 5.

161. A method according to claim 143 wherein the somatostatin agonist has a higher binding affinity for two or more of human somatostatin sub-type receptor 1, human somatostatin sub-type receptor 2, human somatostatin sub-type receptor 3, human somatostatin sub-type receptor 4 or human somatostatin sub-type receptor 5.

162. A method according to claim 143 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof, wherein

A^1 is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, b-Nal, b-Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^2 is Ala, Leu, Ile, Val, Nle, Phe, b-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^3 is pyridyl-Ala, Trp, Phe, b-Nal, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^6 is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A^7 is Ala, Leu, Ile, Val, Nle, Phe, b-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^8 is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, b-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

each R_1 and R_2, independently, is H, lower acyl or lower alkyl; and R_3 is OH or NH_2; provided that at least one of A^1 and A^8 and one of A^2 and A^7 must be an aromatic amino acid; and further provided that A^1, A^2, A^7 and A^8 cannot all be aromatic amino acids.

163. A method according to claim 143 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH_2;

H-D-Phe-p-NO_2-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-b-D-Nal-NH_2;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-b-Nal-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys-b-Nal-NH_2;

D-b-Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH_2;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Ac-D-Phe-Lys*-Tyr-D-Trp-Lys-Val-Asp-Thr-NH_2, wherein an amide bridge is between Lys* and Asp;

Ac-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-L-hArg(Et)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

Ac-L-hArg(CH_2-CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHEt;

Ac-hArg(CH_3, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-hArg(hexyl$_2$)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Propionyl-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys(iPr)-Thr-Cys-Thr-NH_2;

Ac-D-J-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg(Et)$_2$-NH_2;

Ac-D-Lys(iPr)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Ac-D-hArg(Et)$_2$-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-b-Nal-NH_2;

H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Ac-D-b-Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-Phe-Cys-b-Nal-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH_2;

cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe);

cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe);

cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe);

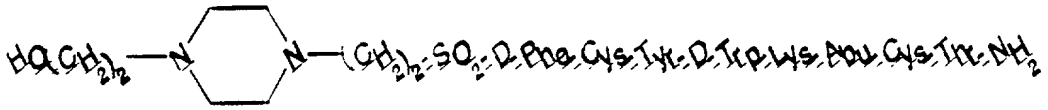
cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe);

cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Ser-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe);
cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr);
cyclo (Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Pro-Phe-D-Trp-4-Amphe-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba);
cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH$(CH_2)_4$CO);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-b-Ala);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp(NO_2)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba);
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba);
cyclo (Phe-Phe-D-Trp(5F)-Lys-Thr-Phe-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-$(CH_2)_3$-CO);

cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
D-b-Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH_2;
H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH_2;



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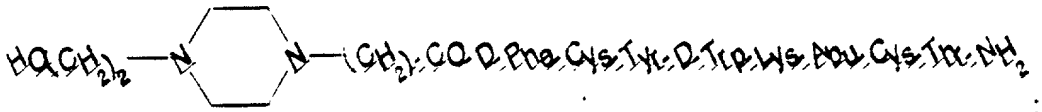

;

or D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys)-Thr-ol; or
a pharmaceutically acceptable salt thereof.

164. A method according to claim 145 wherein the fibrosis induced by a drug or a combination of drugs is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, or in the gastro-intestinal system.

165. A method according to claim 145 wherein the fibrosis induced by a disease state is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, or in the gastro-intestinal system.

166. A method according to claim 145 wherein the fibrosis induced by an environmental or an industrial factor is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, or in the gastro-intestinal system.

167. A method according to claim 145 wherein the fibrosis induced by an immune reaction is in the kidney, in the lung, in the liver, in the skin of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, in the gastro-intestinal system.

168. A method according to claim 145 wherein the fibrosis induced by a wound is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, or in the gastrointestinal system.

169. A pharmaceutical composition useful for inhibiting fibrosis in a patient which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

170. A pharmaceutical composition according to claim 169 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof.

171. A pharmaceutical composition useful for inhibiting overexpression of TGF-J which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

172. A pharmaceutical composition according to claim 171 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof. --

REMARKS

Claims 1 through 141 have been cancelled and claims 142 through 172 have been added. Replacement pages 39 through 52 of new claims are provided for the examiner's convenience. No new matter has been added by the above amendments. Please apply any charges not covered to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 3-1-99

Y. Rocky Tsao
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358155.B11

CLAIMS

What is claimed is:

142. A method of inhibiting fibrosis in a patient said method comprising administering a therapeutically effective amount of somatostatin or a somatostatin agonist to said patient.

143. A method of claim 142, wherein said method comprises administering a therapeutically effective amount of a somatostatin agonist to said patient.

144. A method of claim 143, wherein said fibrosis is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ and or in the gastro-intestinal system.

145. A method of claim 143, wherein said fibrosis is induced by chemotherapy, induced by radiation, induced by a drug or a combination of drugs, induced by a disease state, induced by an environmental or an industrial factor, induced by an immune reaction, or induced by a wound.

146. A method of claim 143, wherein said somatostatin agonist is administered parenterally.

147. A method of claim 146, wherein said somatostatin agonist is administered in a sustained release formulation.

148. A method of claim 144, wherein said somatostatin agonist is administered parenterally.

149. A method of claim 148, wherein said somatostatin agonist is administered in a sustained release formulation.

150. A method of claim 143, wherein said somatostatin agonist is administered topically or orally.

151. A method according to claim 144 wherein the fibrotic disorder in the kidney is glomerulonephritis, diabetic nephropathy, allograft rejection or HIV nephropathy; the fibrotic disorder in the lung is idiopathic fibrosis or

autoimmune fibrosis; the fibrotic disorder in the liver is cirrhosis or veno-occlusive disease; the fibrotic disorder in the skin is systemic sclerosis, keloids, burn scars or eosinophilia-myalgia syndrome and the fibrotic disorder in the central nervous system is intraocular fibrosis.

152. A method according to claim 145 wherein the fibrosis induced by chemotherapy is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ or in the gastro-intestinal system.

153. A method according to claim 145 wherein the fibrosis induced by radiation is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ or in the gastro-intestinal system.

154. A method of inhibiting over-expression of TGF-J which comprises administering to a subject an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

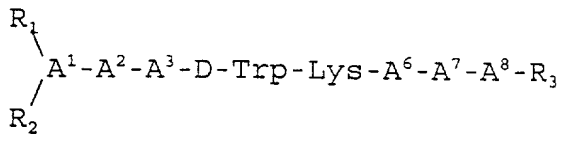
155. A method according to claim 154 wherein a somatostatin agonist or a pharmaceutically acceptable salt thereof is administered.

156. A method according to claim 155 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1, has a higher binding affinity for human somatostatin sub-type receptor 2, has a higher binding affinity for human somatostatin sub-type receptor 3, has a higher binding affinity for human somatostatin sub-type receptor 4, or has a higher binding affinity for human somatostatin sub-type receptor 5.

157. A method according to claim 155 wherein the somatostatin agonist has a higher binding affinity for two or more of human somatostatin sub-type receptor 1, human somatostatin sub-type receptor 2, human somatostatin sub-type

receptor 3, human somatostatin sub-type receptor 4 or human somatostatin sub-type receptor 5.

158. A method according to claim 155 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof, wherein

A^1 is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, J-Nal, J-Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^2 is Ala, Leu, Ile, Val, Nle, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^3 is pyridyl-Ala, Trp, Phe, J-Nal, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^6 is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A^7 is Ala, Leu, Ile, Val, Nle, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^8 is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

each R_1 and R_2, independently, is H, lower acyl or lower alkyl; and R_3 is OH or NH_2; provided that at least one of A^1 and A^8 and one of A^2 and A^7 must be an aromatic amino acid; and further provided that A^1, A^2, A^7 and A^8 cannot all be aromatic amino acids.

159. A method according to claim 155 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH_2;

H-D-Phe-p-NO_2-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-J-D-Nal-NH_2;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-b-Nal-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys-b-Nal-NH_2;

D-b-Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH_2;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Ac-D-Phe-Lys*-Tyr-D-Trp-Lys-Val-Asp-Thr-NH_2, wherein an amide bridge is between Lys* and Asp;

Ac-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-L-hArg(Et)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

Ac-L-hArg(CH_2-CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHEt;

Ac-hArg(CH_3, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-hArg(hexyl$_2$)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Propionyl-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys(iPr)-Thr-Cys-Thr-NH_2;

Ac-D-J-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg(Et)$_2$-NH_2;

Ac-D-Lys(iPr)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Ac-D-hArg(Et)$_2$-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-b-Nal-NH_2;

H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Ac-D-b-Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH_2;

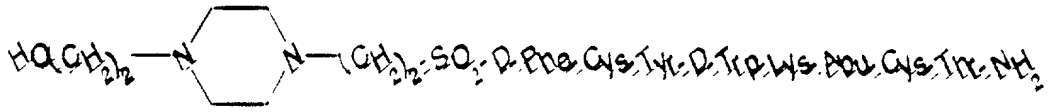
H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;
Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;
H-D-Phe-Cys-b-Nal-D-Trp-Lys-Val-Cys-Thr-NH_2;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH_2;
cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe);
cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe);
cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Ser-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe);
cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr);
cyclo (Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Pro-Phe-D-Trp-4-Amphe-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba);
cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH$(CH_2)_4$CO);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-b-Ala);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);

cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp(NO_2)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba);
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba);
cyclo (Phe-Phe-D-Trp(5F)-Lys-Thr-Phe-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-$(CH_2)_3$-CO);
cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
D-b-Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH_2;
H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH_2;



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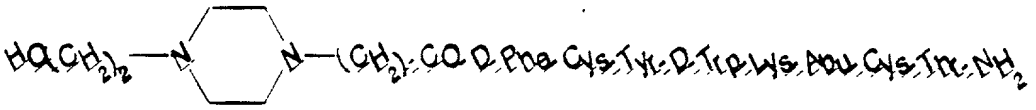

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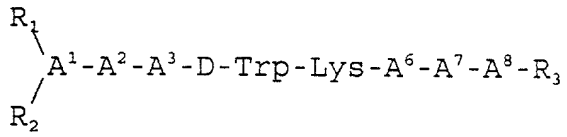
or D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys)-Thr-ol; or a pharmaceutically acceptable salt thereof.

160. A method according to claim 143 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1, has a higher binding affinity for human somatostatin sub-type receptor 2, has a higher binding affinity for human somatostatin sub-type receptor 3, has a higher binding affinity for human somatostatin sub-type receptor 4, or has a higher binding affinity for human somatostatin sub-type receptor 5.

161. A method according to claim 143 wherein the somatostatin agonist has a higher binding affinity for two or more of human somatostatin sub-type receptor 1, human somatostatin sub-type receptor 2, human somatostatin sub-type receptor 3, human somatostatin sub-type receptor 4 or human somatostatin sub-type receptor 5.

162. A method according to claim 143 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof, wherein

A^1 is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, b-Nal, b-Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^2 is Ala, Leu, Ile, Val, Nle, Phe, b-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^3 is pyridyl-Ala, Trp, Phe, b-Nal, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^6 is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A^7 is Ala, Leu, Ile, Val, Nle, Phe, b-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe,

wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

A^8 is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, b-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3, Cl, Br, F, OH, OCH_3 or NO_2;

each R_1 and R_2, independently, is H, lower acyl or lower alkyl; and R_3 is OH or NH_2; provided that at least one of A^1 and A^8 and one of A^2 and A^7 must be an aromatic amino acid; and further provided that A^1, A^2, A^7 and A^8 cannot all be aromatic amino acids.

163. A method according to claim 143 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH_2;

H-D-Phe-p-NO_2-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2;

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-b-D-Nal-NH_2;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-b-Nal-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys-b-Nal-NH_2;

D-b-Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH_2;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH_2;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Ac-D-Phe-Lys*-Tyr-D-Trp-Lys-Val-Asp-Thr-NH_2, wherein an amide bridge is between Lys* and Asp;

Ac-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-L-hArg(Et)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

Ac-L-hArg(CH_2-CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHEt;

Ac-hArg(CH_3, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

H-hArg(hexyl$_2$)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

Ac-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Propionyl-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys(iPr)-Thr-Cys-Thr-NH_2;

Ac-D-J-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg(Et)$_2$-NH_2;

Ac-D-Lys(iPr)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-D-hArg(CH_2CF_3)$_2$-D-hArg(CH_2CF_3)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH_2;

Ac-D-hArg(Et)$_2$-D-hArg(Et)$_2$-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2;

Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH_2;

Bmp-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-b-Nal-NH_2;

H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2;

Ac-D-b-Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH_2;

H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2;

H-D-Phe-Cys-b-Nal-D-Trp-Lys-Val-Cys-Thr-NH_2;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH_2;

cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe);

cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe);

cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe);

cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe);

cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Ser-Phe);

cyclo (Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe);

cyclo (D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe);

cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe);

cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe);

cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr);

cyclo (Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);

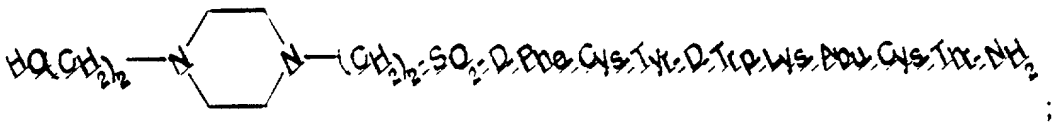
cyclo (Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe);

cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe);

cyclo (N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);

cyclo (Pro-Tyr-D-Trp-4-Amphe-Thr-Phe);

cyclo (Pro-Phe-D-Trp-4-Amphe-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba);
cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH$(CH_2)_4$CO);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-b-Ala);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp(NO_2)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba);
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys)-OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba);
cyclo (Phe-Phe-D-Trp(5F)-Lys-Thr-Phe-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-$(CH_2)_3$-CO);
cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
D-b-Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH_2;
H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH_2;



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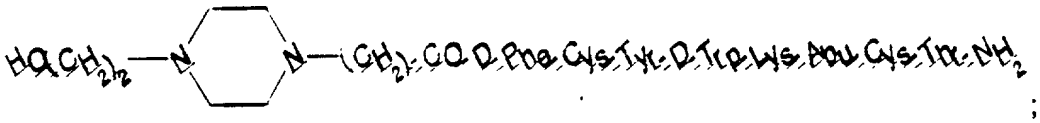

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or D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys)-Thr-ol; or a pharmaceutically acceptable salt thereof.

164. A method according to claim 145 wherein the fibrosis induced by a drug or a combination of drugs is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, or in the gastro-intestinal system.

165. A method according to claim 145 wherein the fibrosis induced by a disease state is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, or in the gastro-intestinal system.

166. A method according to claim 145 wherein the fibrosis induced by an environmental or an industrial factor is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, or in the gastro-intestinal system.

167. A method according to claim 145 wherein the fibrosis induced by an immune reaction is in the kidney, in the lung, in the liver, in the skin of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ, in the gastro-intestinal system.

168. A method according to claim 145 wherein the fibrosis induced by a wound is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone

marrow, in the cardiovascular system, in an endocrine organ, or in the gastrointestinal system.

169. A pharmaceutical composition useful for inhibiting fibrosis in a patient which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

170. A pharmaceutical composition according to claim 169 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof.

171. A pharmaceutical composition useful for inhibiting overexpression of TGF-J which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

172. A pharmaceutical composition according to claim 171 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof.